AMD11070

Drug Description

AMD11070 is an investigational CXCR4 inhibitor. [1]

HIV/AIDS-Related Uses

AMD11070 is an investigational agent with in vitro activity against HIV-1. The safety, tolerability, and pharmacokinetics of AMD11070 are being studied in clinical trials. [2]

Pharmacology

AMD11070 prevents viral entry into cells by binding to the chemokine receptor CXCR4, the co-receptor used by T-cell tropic (X4), syncytium-inducing HIV viruses for membrane fusion and viral entry. AMD11070 does not bind to CCR5, which mediates entry of macrophage-tropic (R5), nonsyncytium-inducing HIV viruses. The X4 strains are considerably more pathogenic; their appearance late in HIV infection correlates with CD4 count decline and rapid disease progression.

AMD11070 has not yet been fully evaluated in human trials. All pharmacokinetic data are from studies in the rat and dog. AMD11070 is rapidly absorbed following oral administration and has an elimination half-life of approximately 10 hours in both rats and dogs. Oral bioavailability is 20% in rats and 80% in dogs. Peak plasma levels are achieved 1 to 2 hours after administration. Bioavailability is significantly reduced when AMD11070 is administered 30 minutes after feeding.

Limited information is available concerning metabolism of AMD11070. AMD11070 represents the major circulating form of the drug in plasma. Preliminary studies indicate the AMD11070 may be a substrate for CYP3A4 and p-glycoprotein. AMD11070 is 84% to 97% protein bound at pharmacologically active concentrations; however, protein binding does not appear to have a significant effect in vitro.

With short-term administration, there is a potential for acute gastrointestinal toxicity characterized by vomiting and diarrhea, usually within 1 to 2 hours of administration. These effects are expected to be transient. Bone marrow hypocellularity has been observed at the highest dose levels; reversibility of this effect has not been demonstrated. Lymphoid atrophy has been observed in the thymus, lymph nodes, and spleen. Heart rate elevations and blood pressure changes have also been noted. AMD11070 is not mutagenic in vitro; however, CXCR4 may play a role in hematopoiesis in utero. Because no information concerning the reproductive toxicity of AMD11070 is currently available, AMD11070 is not being tested in women at this time, and male volunteers in AMD11070 clinical trials are advised to avoid participating in conception activities during AMD11070 administration and for 2 weeks after stopping the drug. [3]

Drug and Food Interactions

In animal studies, the bioavailability of AMD11070 was substantially reduced when the drug was administered 30 minutes after a meal. Current studies are investigating AMD11070 when administered both on an empty stomach and with food.[4]

In a Phase II clinical trial in humans, AMD11070 had additive or synergistic antiviral activity when evaluated in combination with other known HIV inhibitors, including fusion inhibitors (T-20), nucleoside reverse transcriptase inhibitors (zidovudine, tenofovir), and protease inhibitors (amprenavir).[5]

Clinical Trials

For information on clinical trials that involve AMD11070, visit the ClinicalTrials.gov web site at http://www.clinicaltrials.gov. In the Search box, enter: AMD11070 AND HIV Infections.

Dosing Information

Mode of Delivery: Oral.[6]

Dosage Form: AMD11070 is formulated in 25 mg

AMD11070

Dosing Information (cont.)

and 100 mg capsules.[7]

Storage: Store at 2 to 8 C (36 to 46 F).[8]

Chemistry

Physical Description: Solid crystalline.[9]

Other Names

AMD070[10]

Manufacturer Information

AMD11070
AnorMED Inc.
#200-20353 64th Avenue
Langley, BC Canada
604-530-1057

For More Information

Contact your doctor or an AIDSinfo Health Information Specialist:

• Via Phone: 1-800-448-0440 Monday - Friday, 12:00 p.m. (Noon) - 5:00 p.m. ET

• Via Live Help: http://aidsinfo.nih.gov/live_help Monday - Friday, 12:00 p.m. (Noon) - 4:00 p.m. ET

References

1. Protocol ID: ACTG A5191 -

2. Protocol ID: ACTG A5191 -

3. Protocol ID: ACTG A5191 -

4. Protocol ID: ACTG A5191 -

5. Conf Retroviruses Opportunistic Infect. - 10th; February 2003. Abstract 563.

6. Protocol ID: ACTG A5191 -

7. Protocol ID: ACTG A5191 -

8. Protocol ID: ACTG A5191 -

9. Protocol ID: ACTG A5191 -

10. Protocol ID: ACTG A5191 -